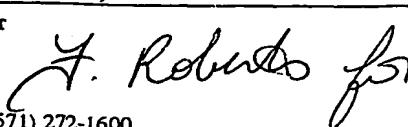


PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)
(PCT Article 36 and Rule 70)

RECD	04 APR 2005
WIPO	PCT

Applicant's or agent's file reference PU60030	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/US04/02425	International filing date (day/month/year) 29 January 2004 (29.01.2004)	Priority date (day/month/year) 30 January 2003 (30.01.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/496; C07D 401/06. and US Cl.: 514/253.06; 544/363		
Applicant SMITHKLINE BEECHAM CORPORATION		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 10%;">Box No. I</td> <td style="width: 80%;">Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand 25 August 2004 (25.08.2004)	Date of completion of this report 21 March 2005 (21.03.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	<p>Authorized officer Emily Bernhardt  Telephone No. (571) 272-1600</p>

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

international search (under Rules 12.3 and 23.1(b))
 publication of the international application (under Rule 12.4)
 international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

the international application as originally filed/furnished

the description:

pages 1-34 as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____

the claims:

pages 35-38 as originally filed/furnished
 pages* NONE as amended (together with any statement) under Article 19
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____

the drawings:

pages NONE as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____

a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. The amendments have resulted in the cancellation of:

the description, pages _____
 the claims, Nos. _____
 the drawings, sheets/figs _____
 the sequence listing (specify): _____
 any table(s) related to the sequence listing (specify): _____

4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

the description, pages _____
 the claims, Nos. _____
 the drawings, sheets/figs _____
 the sequence listing (specify): _____
 any table(s) related to the sequence listing (specify): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/02

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>9</u>	YES
	Claims <u>1-8, 10-12</u>	NO
Industrial Applicability (IA)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-8, and 10-12 lack an inventive step under PCT Article 33(3) as being obvious over Glaxosmithkline Spa (WO 02/44165165). The WO publication describes similar compounds to that claimed herein for the same uses as herein, namely treating respiratory diseases. See pages 2-4 and 2-phenyl species on page 107 last two species in particular. Said species differ only in lacking an oxo group on piperazine carbon(s). However the WO publication describes oxo as a choice as can be seen for the definition of R18 on page 4. Claims 4 and 6 also lack an inventive step since the substituents required in these claims, namely R3 as methyl and one or more fluorines on R4 phenyl are also described in the WO publication as suitable alternatives to esters, amides exemplified. See definitions for R5 and R9 on page 4. The same process of making is also taught on pages 21-22. Thus it would have been obvious to modify the species pointed out above by replacing substituents thereon with those claimed herein in view of the equivalency teachings outlined above and preparation of such an obvious expedient in view of the teachings in the WO publication.

Claim 9 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the type of amides present in the species of this claim.

Claims 1-12 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. Compounds are described for a variety of uses based on activity as NK2 and NK3 antagonists.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International Application No.

PCT/US04/02425

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 4 and 10 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims are indefinite for the following reason(s):

- 1). In claim 4 "R3 or methyl" makes no sense. It appears "or" should be replaced by "is" ;
- 2). In claim 10 the definition of X' is recited as being the same as "X" in claim 1 but there is no "X" in claim 1 and thus scope of X' is unknown.